Cytotoxic chemotherapy

Patients whose tumors have progressed on hormone therapy are candidates for cytotoxic chemotherapy. Patients with hormone receptor-negative tumors and those with visceral metastases are also candidates for cytotoxic agents.

Single agents that have shown activity in metastatic breast cancer:

- Anthracyclines.
  - Doxorubicin.
  - Epirubicin.
  - Liposomal doxorubicin.[50-52]
  - Mitoxantrone.
- Taxanes.
  - Paclitaxel.
  - Docetaxel.
  - Albumin-bound nanoparticle paclitaxel (ABI-007 or Abraxane).[53]
- Alkylating agents.
  - Cyclophosphamide.
- Fluoropyrimidines.
  - Capecitabine.[54,55]
  - 5-FU.
- Antimetabolites.
  - Methotrexate.
- Vinca alkaloids.
  - Vinorelbine.[56]
  - Vinblastine.
  - Vincristine.
- Platinum.
  - Carboplatin.
  - Cisplatin.
- Other.
  - Gemcitabine.[57]
  - Mitomycin C.

Combination regimens that have shown activity in metastatic breast cancer:

- CA: cyclophosphamide and doxorubicin.[58]
- Docetaxel and doxorubicin.[59]
- CAF: cyclophosphamide, doxorubicin, 5-fluorouracil.[60]
- CMF: cyclophosphamide, methotrexate, 5-fluorouracil.[61]
- Doxorubicin and paclitaxel.[62,63]
- Docetaxel and capecitabine.[64]
- Vinorelbine and epirubicin.[65]

EXHIBIT A